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OC-0070: 18F-FDG PET image biomarkers improve prediction of late radiation-induced xerostomia

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OC-0069 Influence of PET radiomics implementation on reproducibility of tumor control prognostic models

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Purpose or Objective

Radiomics is a powerful tool for tumor characterization. However, the lack of the standardization in different radiomics implementations can be a cause of model irreproducibility. The aim of this study was to correlate local tumor control in head and neck squamous cell carcinoma (HNSCC) with post-radiochemotherapy (RCT) PET radiomics and test the obtained models against two independent radiomics implementations on a clinically relevant data set.

Material and Methods

HNSCC patients, who underwent a follow-up 18F-FDG PET scan 3 months post definitive RCT, were retrospectively included in the study (training cohort n=149, validation cohort=53). Tumors were semi-automatically segmented on the pre-treatment 18F-FDG PET using a gradient-based method and transferred to post-RCT scans. Radiomic features were extracted using two independent software implementations: in-house implementation from University Hospital Zurich (USZ) and Radiomics from MAASTRO. In total, 674 features, available in the both implementations and based on the same definitions, comprising: shape (n=8), intensity (n=16), texture (n=58) and wavelet transform (n=592) were compared using the intraclass correlation coefficient (ICC). Two separate models were built selecting features from either USZ or MAASTRO implementation. Redundant features were excluded in a principal component analysis. The best performing features based on univariable Cox regression were included in the multivariable analysis with backward selection of the variables using Akaike information criterion. The quality of models was assessed using the concordance index (CI). The performance of both models was tested on the training data using features from the other implementation as well as on the validation data using features obtained with both implementations. The performance was also evaluated on the patient level by the comparison of the patient ranking from two implementations using Pearson correlation.

Results

Only 71 PET radiomic features yielded ICC > 0.8 in the comparison between the two implementations. The wavelet features showed the biggest discrepancy. The features comprised in the two prognostic models were different between the two radiomics implementations. However, both models showed a good performance when corresponding features from the other implementation were used (Table 1). Both models performed equally well in the validation cohort for both radiomics implementations (CI: 0.67-0.71). However, features from different implementations resulted in altered patient ranking. In one of the models the ranks showed strong correlation ($r_{\text{training}}=0.89$, $r_{\text{validation}}=0.85$), whereas in the second the correlation was weak ($r_{\text{training}}=0.62$, $r_{\text{validation}}=0.45$) as more features characterized by low ICC were present.

Table 1. Performance of PET radiomics models for prediction of local tumor control and the stability of radiomic features between two radiomics implementations. CI – concordance index, ICC – intraclass correlation coefficient, MAASTRO and USZ two independent radiomics implementations.

Model developed using radiomic features from	Model radiomic features	ICC	CI training		CI validation	
			MAASTRO	USZ	MAASTRO	USZ
MAASTRO	HLL GLRLMrunge	0.20	0.81	0.72	0.69	0.67
	LHL GLCMsum_entropy	0.59				
	LHH GLCM_autocorrelation	0.03				
	LHL GLCMcluster_prominence	<0.01				
USZ	Histogramstandard_deviation	0.98	0.75	0.75	0.69	0.71
	GLRLMglv	0.97				
	GLCMcluster_prominence	0.96				
	Histograminterquartile_range	0.94				
	LHL GLRLMhore	0.11				

Conclusion

The two post-RCT PET radiomic models for local tumor control preserved their prognostic power using independent radiomics implementation. However, the significant differences in patient rankings were observed.

OC-0070 18F-FDG PET image biomarkers improve prediction of late radiation-induced xerostomia

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Purpose or Objective

Current prediction of radiation-induced xerostomia 12 months after radiotherapy (Xer_{12m}) is based on mean parotid gland dose and baseline xerostomia scores. Our hypothesis is that the development of xerostomia is associated with patient-specific information from ¹⁸F-FDG PET images that is quantified in PET image biomarkers (PET-IBMs). The purpose of this study is to improve prediction of Xer_{12m} with these PET-IBMs.

Material and Methods

¹⁸F-FDG PET images of 161 head and neck cancer patients were acquired before start of treatment. From these images, SUV-intensity (17) and textural (63) PET-IBMs of the parotid gland were extracted. In addition, XER-base, tumour, patient characteristics and mean doses to the parotid gland were considered. Patient-rated toxicity (Xer_{12m}) was prospectively collected (EORTC QLQ-H&N35). PET-IBMs were selected using a forward step-wise variable selection procedure. The resulting logistic regression models with the selected PET-IBMs were compared with the reference model that was based on parotid gland dose and baseline xerostomia only. All models were internally validated by bootstrapping.

Results

Sixty (37%) patients developed moderate-to-severe Xer_{12m}. The 90th percentile of SUVs (P90) in the parotid gland of the intensity PET-IBMs was selected and was significantly associated with Xer_{12m} ($p<0.001$). The P90 significantly improved model performance of the reference model in predicting Xer_{12m} (see Table 1: Likelihood-ratio test) from an AUC = 0.73 (reference model) to 0.77 (P90 added). Similar improvement was obtained from Long Run High Gray-level Emphasis 2 (LRHG2E) of the textural PET-IBMs (Table 1), which was significantly correlated with P90 ($p=0.83$). The PET-IBMs P90 and LRHG2E both had high values with high SUVs present in the parotid gland. More specifically, P90 indicates the minimum value of the 90th highest SUV values and the LRHG2E indicated high SUV values that are spatially adjacent to each other (Figure). Both PET-IBMs were negatively associated with Xer_{12m}, suggesting that patients with low metabolic activity in the parotid glands were at risk of developing late xerostomia.

Since both P90 and LRHG2E have similar performance, P90 is preferred due to its calculation simplicity compared to LRHG2E.

Conclusion

Prediction of Xer_{12m} was significantly improved with 90th percentile of SUVs, indicating that low metabolic activity of the parotid gland was associated with the risk of developing xerostomia after radiotherapy. This study highlights the importance of incorporating patient-specific functional characteristics into NTCP model development.

OC-0071 Clustering of multi-parametric functional imaging: identifying high risk subvolumes in NSCLC tumours

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Purpose or Objective

Tumours are heterogeneous. Characteristics such as metabolic activity, proliferation, cell death and vasculature vary throughout a tumour, influencing the sensitivity to (radio)therapy. Biomarkers predicting patient prognosis often neglect these subpopulation heterogeneities and rarely take spatial differences into account. This study aimed to identify tumour subregions with characteristic phenotypes and to correlate these subregions to treatment outcome using functional imaging for metabolic activity (FDG PET/CT), hypoxia (HX4 PET/CT), and tumour vasculature (DCE-CT).

Material and Methods

For 32 non-small cell lung cancer (NSCLC) patients, a planning FDG PET/CT, hypoxia PET/CT and DCE-CT scan were acquired before the start of radiotherapy. Kinetic analysis was performed on the DCE-CT to acquire parametric maps of blood volume (BV). HX4 PET/CT and DCE-CT scans were non-rigidly deformed to the planning (PET/CT). Similar voxels within the gross tumour volume (GTV) of the planning CT scan were grouped using a SLIC algorithm (Achanta, 2012) to create spatially independent 3D subregions (i.e. supervoxels), and to account for registration uncertainties. Inside these supervoxels, the median values of FDG SUV, HX4 SUV and BV were calculated, see Figure 1. Next, an unsupervised hierarchical clustering algorithm was used to group supervoxels of all patients. The number of clusters was based on the gap metric. Overall survival was assessed using Kaplan-Meier curves. Furthermore, patients were split into two cohorts based on median survival and individual supervoxels of all patients were compared.

Results

Supervoxels could be generated for 29 out of 32 patients with a small GTV volume hindering analysis on the other 3 patients. Unsupervised clustering of all supervoxels over all patients provided 4 independent groups. The red cluster (high BV, low/intermediate FDG, intermediate HX4) related to a high risk tumour type: patients presenting supervoxels in this cluster had significantly worse survival compared to patients that did not ($p=0.037$; c-index Cox model=0.626), Figure 1. Figure 2 shows the supervoxels of all patients separated into survival larger than the median (=18 months) (green dots) or lower (red dots). Large values (e.g. outliers) in HX4 and FDG uptake corresponded to worse performing patients, while intermediate values (possibly corresponding to more homogeneous areas) were related to a good prognosis. The same was found for BV (not shown).

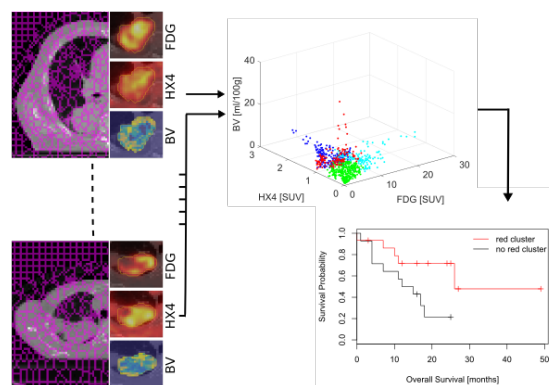


Figure 1. Workflow: supervoxels, clustering and Kaplan-Meier curves for red cluster.

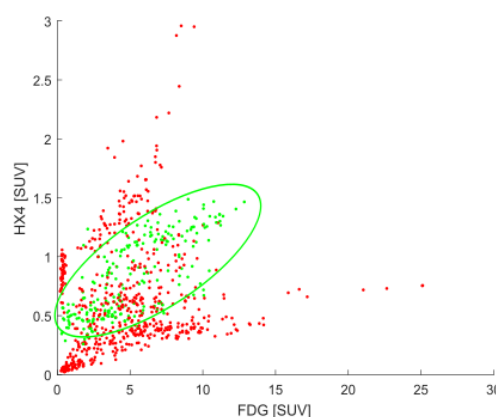


Figure 2. Supervoxels of patients with a survival larger (green) or lower (red) than the median overall survival.

Conclusion

We designed a methodology for the analysis of multi-parametric imaging data in NSCLC patients on sub-regional level. We showed that such an intra-tumour classification of heterogeneous subregions may allow to predict patient prognosis. This technique allows to gain further insight into the analysis of multi-parametric functional images.

Proffered Papers: Improvements in positioning and motion management

OC-0072 4D-MRI based evaluation of moving lung tumor target volumes

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